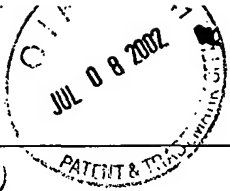


5000  
6/17/02



525 Rec'd PCT/PTC 08 JUL 2002

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Arlington, VA 22202, on the date appearing below.

ELI LILLY AND COMPANY

By Hinda M. Durbin Date July 2, 2002

**PATENT APPLICATION**  
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants : Gerald Wayne Becker, *et al.* )  
Serial No. : 10/018,383 )  
Filed : October 30, 2001 )  
For : AMYLOID PRECURSOR PROTEIN ) Confirmation No.:  
PROTEASE AND RELATED ) 7903  
NUCLEIC ACID COMPOUNDS )  
Docket No. : X-11600 )

**RESPONSE TO NOTIFICATION OF DEFECTIVE RESPONSE**

Assistant Commissioner for Patents  
Arlington, VA 22202  
Attention: Box Sequence  
Sir:

This is in response to a "Notification of Defective Response" dated June 13, 2002, noting the absence of an acceptable Sequence Listing.

Enclosed herewith are:

- 1) a copy of the Notification;
- 2) a computer-readable copy of the Sequence Listing pursuant to 37 C.F.R. § 1.821(e);
- 3) a paper copy of the Sequence Listing pursuant to 37 C.F.R. § 1.821(c);

**DISK TO STIC**

DATE: \_\_\_\_\_



Serial No. 10/018,383

- 4) an affirmation pursuant to 37 C.F.R. § 1.821(f);
- 5) a Supplemental Preliminary Amendment amending the specification to include the sequence listing;
- 6) an Information Disclosure Statement; and
- 7) a Form PTO-1449 (modified).

Respectfully submitted,

*Paula K. Davis*

Paula K. Davis  
Agent for Applicants  
Registration No. 47,517  
Phone: 317-433-3422

Eli Lilly and Company  
Patent Division  
P.O. Box 6288  
Indianapolis, Indiana 46206-6288

02 July 2002



UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents, Box PCT  
 United States Patent and Trademark Office  
 Washington, D.C. 20231  
 www.uspto.gov

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/018,383	Gerald Wayne Becker	X-11600
INTERNATIONAL APPLICATION NO.		
PCT/US00/06707		
I.A. FILING DATE	PRIORITY DATE	
05/09/2000	05/11/1999	

Eli Lilly and Company  
 Patent Division/PKD  
 Lilly Corporation Center  
 Indianapolis, IN 46285

CONFIRMATION NO. 7903

371 FORMALITIES LETTER

\*OC000000008278122\*

Date Mailed: 06/13/2002

### NOTIFICATION OF DEFECTIVE RESPONSE

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as an Elected Office (37 CFR 1.495):

- U.S. Basic National Fee
- Priority Document
- Assignee Statement
- Biochemical Sequence Diskette
- Biochemical Sequence Listing
- Copy of IPE Report
- Copy of references cited in ISR
- Copy of the International Application
- Copy of the International Search Report
- Oath or Declaration
- Preliminary Amendments

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

**Applicant is required to complete the response within a time limit of ONE MONTH from the date of this Notification or within the time remaining in the response set forth in the Notification of Missing Requirements, whichever is the longer. No extension of this time limit may be granted under 37 CFR 1.136, but the period for response set in the Notification of Missing Requirements may be extended under 37 CFR 1.136(a).**

The following items **MUST** be furnished within the period set forth below:

- The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821-1.825 for the following reason(s):
  - A copy of the "Sequence Listing" in computer readable form has been submitted. The content of the computer readable form, however, does not comply with the requirements of 37 CFR 1.822 and/or 1.832, as indicated on the attached marked-up copy of the "Raw Sequence Listing."

- The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).
  - APPLICANT MUST PROVIDE:
    - An initial or substitute computer readable form (CRF) of the "Sequence Listing."
    - An initial or substitute paper copy or compact disc of the "Sequence Listing," as well as an amendment directing its entry into the specification.
- For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:
- For Rules Interpretation, call (703) 308-4216
  - To Purchase PatentIn Software, call (703) 306-2600
  - For PatentIn Software Program Help, call (703) 306-4119 or e-mail at [patin21help@uspto.gov](mailto:patin21help@uspto.gov) or [patin3help@uspto.gov](mailto:patin3help@uspto.gov)
- A copy of the "Sequence Listing" in computer readable form has been submitted. The content of the computer readable form, however, does not comply with the requirements of 37 CFR 1.822 and/or 1.832, as indicated on the attached marked-up copy of the "Raw Sequence Listing."
  - The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

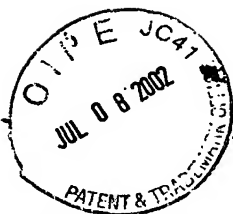
*A copy of this notice **MUST** be returned with the response.*

VONDA M WALLACE

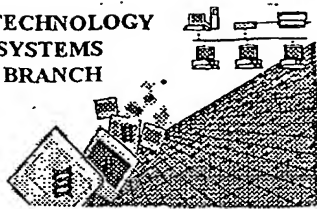
Telephone: (703) 305-3736

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/018,383	PCT/US00/06707	X-11600



BIOTECHNOLOGY  
SYSTEMS  
BRANCH



**RAW SEQUENCE LISTING  
ERROR REPORT**

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/018,383  
Source: PCR/10  
Date Processed by STIC: 6/4/2002

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: [patin21help@uspto.gov](mailto:patin21help@uspto.gov) or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: [patin3help@uspto.gov](mailto:patin3help@uspto.gov) or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER** VERSION 3.1 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>>, EFS Submission User Manual - ePAVE)

2. U.S. Postal Service: U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202

3. Hand Carry directly to:

U.S. Patent and Trademark Office, Technology Center 1600, Reception Area, 7<sup>th</sup> Floor, Examiner Name, Sequence Information, Crystal Mall One, 1911 South Clark Street, Arlington, VA 22202

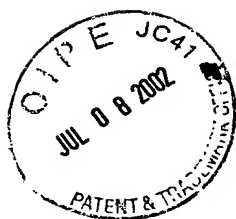
Or

U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office,

Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 01/29/2002



PCT10

RAW SEQUENCE LISTING  
PATENT APPLICATION: US/10/018,383

DATE: 06/04/2002  
TIME: 14:56:06

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Output Set: N:\CRF3\06042002\J018383.raw

Does Not Comply  
Corrected Diskette Needed

pp 3-6

3 <110> APPLICANT: Becker, Gerald  
4 Hale, John  
5 Heath, William  
6 Johnstone, Edward  
7 Little, Sheila  
8 Tu, Yuan  
9 Yeh, Wu-Kuang  
10 Yin, Tinggui  
12 <120> TITLE OF INVENTION: Amyloid Precursor Protein Protease and Related Nucleic Acid Compounds  
14 <130> FILE REFERENCE: X-11600  
C--> 16 <140> CURRENT APPLICATION NUMBER: US/10/018,383  
C--> 16 <141> CURRENT FILING DATE: 2002-03-05  
16 <160> NUMBER OF SEQ ID NOS: 5  
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42 atg ggt gtg cat gtg ggt gca gcc ctg gga gca ctg tgg ttc tgc-99  
43 Met Gly Val His Val Gly Ala Ala Leu Gly Ala Leu Trp Phe Cys-99  
44 10 15 20 25  
46 aca gga gcc ctg gag gtc cag gtc cct gaa gac cca gtg gtg gca-1470  
47 Thr Gly Ala Leu Glu Val Gln Val Pro Glu Asp Pro Val Val Ala-1470  
48 30 35 40  
50 gtg ggc acc gat gcc acc ctg tgc tgc tcc ttc tcc cct gag cct-315195  
51 Val Gly Thr Asp Ala Thr Leu Cys Cys Ser Phe Ser Pro Glu Pro-315195  
52 45 50 55  
54 ttc agc ctg gca cag ctc aac ctc atc tgg cag ctg aca gat acc aaa-243  
55 Phe Ser Leu Ala Gln Leu Asn Leu Ile Trp Gln Leu Thr Asp Thr Lys  
56 60 65 70  
58 cag ctg gtg cac agc ttt gct gag ggc cag gac cag ggc agc gcc tat-291

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/018,383

DATE: 06/04/2002

TIME: 14:56:06

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63 Ala Asn Arg Thr Ala Leu Phe Pro Asp Leu Leu Ala Gln Gly Asn Ala
64 90      95      100      105
66 tcc ctg agg ctg cag cgc gtg cgt gtg gcg gac gag ggc agc ttc acc 387
67 Ser Leu Arg Leu Gln Arg Val Arg Val Ala Asp Glu Gly Ser Phe Thr
68      110      115      120
70 tgc ttc gtg agc atc cgg gat ttc ggc agc gct gcc gtc agc ctg cag 435
71 Cys Phe Val Ser Ile Arg Asp Phe Gly Ser Ala Ala Val Ser Leu Gln
72      125      130      135
74 gtg gcc gct ccc tac tcg aag ccc agc atg acc ctg gag ccc aac aag 483
75 Val Ala Ala Pro Tyr Ser Lys Pro Ser Met Thr Leu Glu Pro Asn Lys
76      140      145      150
78 gac ctg cgc cca ggg gac acg gtg acc atc acg tgc tcc agc tac cag 531
79 Asp Leu Arg Pro Gly Asp Thr Val Thr Ile Thr Cys Ser Ser Tyr Gln
80      155      160      165
82 ggc tac cct gag gct gag gtg ttc tgg cag gat ggg cag ggt gtg ccc 579
83 Gly Tyr Pro Glu Ala Glu Val Phe Trp Gln Asp Gly Gln Gly Val Pro
84 170      175      180      185
86 ctg act ggc aac gtg acc acg tcg cag atg gcc aac gag cag ggc ttg 627
87 Leu Thr Gly Asn Val Thr Thr Ser Gln Met Ala Asn Glu Gln Gly Leu
88      190      195      200
90 ttt gat gtg cac agc atc ctg cgg gtg gtg ctg ggt gca aat ggc acc 675
91 Phe Asp Val His Ser Ile Leu Arg Val Val Leu Gly Ala Asn Gly Thr
92      205      210      215
94 tac agc tgc ctg gtg cgc aac ccc gtg ctg cag cag gat gcg cac agc 723
95 Tyr Ser Cys Leu Val Arg Asn Pro Val Leu Gln Gln Asp Ala His Ser
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98 tot gtc acc atc aca ccc cag aga agc ccc aca gga gcc gtg gag gtc 771
99 Ser Val Thr Ile Thr Pro Gln Arg Ser Pro Thr Gly Ala Val Glu Val
100      235      240      245
102 cag gtc cct gag gac ccg gtg gtg gcc cta gtg ggc acc gat gcc acc 819
103 Gln Val Pro Glu Asp Pro Val Val Ala Leu Val Gly Thr Asp Ala Thr
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107 Leu Arg Cys Ser Phe Ser Pro Glu Pro Gly Phe Ser Leu Ala Gln Leu
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111 Asn Leu Ile Trp Gln Leu Thr Asp Thr Lys Gln Leu Val His Ser Phe 915
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114 acc gaa ggc cgg gac cag ggc agc gcc tat gcc aac cgc acg gcc ctc 963
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118 ttc ccg gac ctg ctg gca caa ggc aat gca tcc ctg agg ctg cag cgc 1011
119 Phe Pro Asp Leu Leu Ala Gln Gly Asn Ala Ser Leu Arg Leu Gln Arg 1011
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123 Val Arg Val Ala Asp Glu Gly Ser Phe Thr Cys Phe Val Ser Ile Arg 1059

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## RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/018,383

DATE: 06/04/2002

TIME: 14:56:06

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126 gat ttc ggc agc gct gcc gtc agc ctg cag gtg gcc gct ccc tac tcg      1107
127 Asp Phe Gly Ser Ala Ala Val Ser Leu Gln Val Ala Ala Pro Tyr Ser
128          350          355          360
130 aag ccc agc atg acc ctg gag ccc aac aag gac ctg cgg cca ggg gac      1155
131 Lys Pro Ser Met Thr Leu Glu Pro Asn Lys Asp Leu Arg Pro Gly Asp
132          365          370          375
134 acg gtg acc atc acg tgc tcc agc tac cgg ggc tac cct gag gct gag      1203
135 Thr Val Thr Ile Thr Cys Ser Ser Tyr Arg Gly Tyr Pro Glu Ala Glu
136          380          385          390
138 gtg ttc tgg cag gat ggg cag ggt gtg ccc ctg act ggc aac gtg acc      1251
139 Val Phe Trp Gln Asp Gly Gln Gly Val Pro Leu Thr Gly Asn Val Thr
140          395          400          405
W--> 142 acg tcg cag atg gcc aac gag cag ggc ttg ttt nnn nnn nnn nnn nnn      1299
W--> 143 Thr Ser Gln Met Ala Asn Glu Gln Gly Leu Phe Xaa Xaa Xaa Xaa Xaa
144 410          415          420          425
W--> 146 nnn nnn nnn nnn nnn nnn nnn nnn nnn nnn nnn nnn nnn nnn nnn      1347
W--> 147 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
148          430          435          440
W--> 150 nnn nnn nnn nnn nnn nnn gat gcg cac ggc tct gtc acc atc aca ggg      1395
W--> 151 Xaa Xaa Xaa Xaa Xaa Xaa Asp Ala His Gly Ser Val Thr Ile Thr Gly
152          445          450          455
154 cag cct atg aca ttc ccc cca gag gcc ctg tgg gtg acc gtg ggg ctg      1443
155 Gln Pro Met Thr Phe Pro Pro Glu Ala Leu Trp Val Thr Val Gly Leu
156          460          465          470
158 tct gtc tgt ctg att gca ctg ctg gtg gcc ctg gct ttc gtg tgc tgg      1491
159 Ser Val Cys Leu Ile Ala Leu Leu Val Ala Leu Ala Phe Val Cys Trp
160          475          480          485
162 aga aag atc aaa cag agc tgt gag gag gag aat gca gga gct gag gac      1539
163 Arg Lys Ile Lys Gln Ser Cys Glu Glu Glu Asn Ala Gly Ala Glu Asp
164 490          495          500          505
166 cag gat ggg gag gga gaa ggc tcc aag aca gcc ctg cag cct ctg aaa      1587
167 Gln Asp Gly Glu Gly Glu Gly Ser Lys Thr Ala Leu Gln Pro Leu Lys
168          510          515          520
170 cac tct gac agc aaa gaa gat gat gga caa gaa ata gcc tga      1629
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186 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon, Tyr, Cys, or Phe
187 Tyr, Trp, Cys, or Phe.
189 <220> FEATURE:

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codon



RAW SEQUENCE LISTING  
 PATENT APPLICATION: US/10/018,383

DATE: 06/04/2002  
 TIME: 14:56:06

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 192 <223> OTHER INFORMATION: The 'Xaa' at location 422 stands for Lys, Asn, Arg, Ser,  
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 200 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
 201 Tyr, Trp, Cys, or Phe.  
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 205 <222> LOCATION: (424)..(424)  
 206 <223> OTHER INFORMATION: The 'Xaa' at location 424 stands for Lys, Asn, Arg, Ser,  
 Thr, Ile  
 207 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
 208 Tyr, Trp, Cys, or Phe.  
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 212 <222> LOCATION: (425)..(425)  
 213 <223> OTHER INFORMATION: The 'Xaa' at location 425 stands for Lys, Asn, Arg, Ser,  
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 214 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
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 235 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
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 240 <222> LOCATION: (429)..(429)  
 241 <223> OTHER INFORMATION: The 'Xaa' at location 429 stands for Lys, Asn, Arg, Ser,  
 Thr, Ile



RAW SEQUENCE LISTING  
PATENT APPLICATION: US/10/018,383

DATE: 06/04/2002  
TIME: 14:56:06

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Output Set: N:\CRF3\06042002\J018383.raw

247 <222> LOCATION: (430)..(430)  
248 <223> OTHER INFORMATION: The 'Xaa' at location 430 stands for Lys, Asn, Arg, Ser,  
Thr, Ile  
249 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
250 Tyr, Trp, Cys, or Phe.  
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254 <222> LOCATION: (431)..(431)  
255 <223> OTHER INFORMATION: The 'Xaa' at location 431 stands for Lys, Asn, Arg, Ser,  
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256 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
257 Tyr, Trp, Cys, or Phe.  
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261 <222> LOCATION: (432)..(432)  
262 <223> OTHER INFORMATION: The 'Xaa' at location 432 stands for Lys, Asn, Arg, Ser,  
Thr, Ile  
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264 Tyr, Trp, Cys, or Phe.  
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271 Tyr, Trp, Cys, or Phe.  
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275 <222> LOCATION: (434)..(434)  
276 <223> OTHER INFORMATION: The 'Xaa' at location 434 stands for Lys, Asn, Arg, Ser,  
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278 Tyr, Trp, Cys, or Phe.  
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291 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,  
292 Tyr, Trp, Cys, or Phe.  
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296 <222> LOCATION: (437)..(437)  
297 <223> OTHER INFORMATION: The 'Xaa' at location 437 stands for Lys, Asn, Arg, Ser,  
Thr, Ile  
298 , Met, Glu, Asp, Gly, Ala, Val, Gln, His, Pro, Leu, a stop codon,

file://C:\Cr3\Outhold\VsJ018383.htm

*Please correct this  
error throughout sequence*

06/04/02

299 Tyr, Trp, Cys, or Phe.  
301 <220> FEATURE:  
302 <221> NAME/KEY: misc\_feature  
303 <222> LOCATION: (438)..(438)

RAW SEQUENCE LISTING ERROR SUMMARY  
PATENT APPLICATION: US/10/018,383

DATE: 06/04/2002  
TIME: 14:56:07

Input Set : A:\X11600.ST25.txt  
Output Set: N:\CRF3\06042002\J018383.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; N Pos. 1285,1286,1287,1288,1289,1290,1291,1292,1293,1294,1295,1296  
Seq#:1; N Pos. 1297,1298,1299,1300,1301,1302,1303,1304,1305,1306,1307,1308  
Seq#:1; N Pos. 1309,1310,1311,1312,1313,1314,1315,1316,1317,1318,1319,1320  
Seq#:1; N Pos. 1321,1322,1323,1324,1325,1326,1327,1328,1329,1330,1331,1332  
Seq#:1; N Pos. 1333,1334,1335,1336,1337,1338,1339,1340,1341,1342,1343,1344  
Seq#:1; N Pos. 1345,1346,1347,1348,1349,1350,1351,1352,1353,1354,1355,1356  
Seq#:1; N Pos. 1357,1358,1359,1360,1361,1362,1363,1364,1365  
Seq#:1; Xaa Pos. 421,422,423,424,425,426,427,428,429,430,431,432,433,434  
Seq#:1; Xaa Pos. 435,436,437,438,439,440,441,442,443,444,445,446,447  
Seq#:2; Xaa Pos. 421,422,423,424,425,426,427,428,429,430,431,432,433,434  
Seq#:2; Xaa Pos. 435,436,437,438,439,440,441,442,443,444,445,446,447